the use of e-health interventions.*Both B. F. M. Wijnen and L. A. M. Leenen contributed equally to this work.

PRM226

IMPLEMENTATION OF INTERNATIONAL CHART REVIEW STUDIES: AN ASSESSMENT OF ETHICS AND REGULATORY CONSIDERATIONS

Jean-Mary J[1], Stein D[2], Yeomans K[2], Payne KA[3]

[1]*United BioSource Corporation, London, UK,* [2]*UBC: An Express Scripts Company, Dorval, QC, Canada,* [3]*United BioSource Corporation, Dorval, QC, Canada*

OBJECTIVES: In the absence of secondary sources of health care data, chart review studies can result in patient level data repositories including patient characteristics, care patterns, treatment effectiveness and clinical and safety outcomes. Data can be used to populate economic evaluations, and value dossiers, and inform drug safety assessments. For successful implementation, however, knowledge of country-specific ethics and regulatory approval processes is paramount. **METHODS:** Operational, ethics and regulatory issues and considerations as well as strategies for study success have been summarized in the context of eleven recent multi-national chart review case studies. **RESULTS:** Two of 11 studies also collected data prospectively; two studies were categorized as post authorization safety studies and three studies were conducted in peri-approval compassionate use program populations. The majority of studies (9) were oncology focused, with two studies focused on infectious diseases and opioid-induced constipation. Sample sizes varied from 20 to 500 patients, the number of countries from 1 to 8, and the number of sites from 4 to 61. All studies included at least one European country. Across studies, key operational considerations that impacted the ethical/regulatory approval process were ambiguous/amorphous multinational regulatory requirements/guidelines; commercial availability or non-availability of the sponsor product at the time of chart abstraction; data collection method(s) (i.e., retrospective vs. hybrid chart review plus prospective data collection); country variation in informed consent requirements and definitions of personal data; and multinational contractual requirements with the participating sites. **CONCLUSIONS:** International chart review studies are an effective methodology to resolve data gaps not solved by existing secondary health care data sources resulting in tailored, patient-level datasets. Current knowledge of the highly variable and evolving global regulatory requirements, as well as the development of a risk management plan informed by methodological and operational lessons learned at study-outset will facilitate risk mitigation and allow researchers to overcome key challenges.

PRM227

COST PER PATIENT IN NON INTERVENTIONAL STUDIES AND ADDED VALUE OF DIRECT TO PATIENT CONTACT SERVICE

Fournie X

Mapi, Lyon, France

OBJECTIVES: In addition to study outcome concerns arising from patients lost to follow-up (LFU) in pharmacoepidemiology and pharmacovigilance studies, the financial impact of LFU can be significant. Our objectives were to estimate cost per patient in Non-interventional studies, to identify variables that may affect this patient cost, to estimate cost of patient lost to follow-up (LFU), and financial benefits that can be expected from LFU minimization through Direct to Patient Contact service (DPC). **METHODS:** Analysis of 2013 proposals and budgets submitted to study sponsors. Selection criteria: non interventional, prospective, longitudinal patient follow-up, full CRO services. Analysis were performed according to patient sample size, study duration, disease category, and different hypothesis for LFU rates. **RESULTS:** 1) 20 studies (Domestic, Regional or Global) met all inclusion criteria; 2) Annual cost per patient -ranging from €1,068 to €4,370- decreases as the study duration increases (set-up cost is more diluted in the patient annual cost). But the longer the study is the more expensive the overall cost per patient; 3) Mean annual patient cost significantly differs according to rarity of disease/population; rarity is an important criterion that greatly impacts overall and annual patient cost, especially for study lasting more than 1 year. Below 1 year, the cost per patient remains quite similar between types of diseases/populations; 4) Cost are more significant in rare diseases studies, therefore DPC can provide the best overall cost savings in these populations; and 50 The cost savings are depended on the expected rate of patient LFU-with/without DPC service and the planned patient sample size. **CONCLUSIONS:** Return On Investment plays an important role for Sponsors to determine if DPC is valuable in a study. The financial investment may be beneficial regardless of the cost to insure completion of the patients, thus meeting the scientific study objectives. But it could generate cost savings as well.

PRM228

RETROSPECTIVE CHART REVIEW STUDIES: STRATEGIES TO ENSURE ROBUST DATA QUALITY

Stein D[1], Bassel M[1], Payne KA[2]

[1]*UBC: An Express Scripts Company, Dorval, QC, Canada,* [2]*United BioSource Corporation, Dorval, QC, Canada*

OBJECTIVES: Retrospective chart review studies can result in robust naturalistic data to inform evaluations of treatment patterns, resource utilization, costs of care, clinical outcomes and safety. Data quality control is challenging both as a result of poor quality documentation in the usual care medical chart, or as a result of data abstraction and data entry processes. **METHODS:** Ten chart review case studies conducted in the United States, Canada and Europe were evaluated to provide recommendations for improving chart review data quality control mechanisms. **RESULTS:** All 10 studies used electronic data capture (EDC) systems. Common lessons learned across the studies were that the case report forms (CRFs) should only include necessary data points required to fulfill the analysis. Direct chart-to-EDC data entry and remote real-time data quality control is recommended to reduce additional transcription errors that may occur if using paper CRFs. It is important to ensure the EDC system includes a cohort-control platform that enables selection of patient cohorts (i.e., random selection) and tracking of eligibility screening to reduce selection bias risk. Automated edit checks of primary data endpoints should be programmed into the EDC system prompting data abstractors to revise erroneous data and/or confirm data outside of expected ranges at entry. To confirm abstracted data reflect source documents (patient medical charts), a second abstractor at the site can re-abstract pre-defined critical study variables from patient medical charts for cross-referencing for data discrepancies. Site training must be effective to ensure compliance with chart abstraction and data quality requirements. **CONCLUSIONS:** Given the frequent incomplete or poor quality medical chart information and the potential for human error in data abstraction and entry processes, data quality control methods are paramount. Approaches to protocol, CRF and study training materials design can positively impact data quality.

RESEARCH ON METHODS – Conceptual Papers

PRM229

RESEARCH PRIORITIZATION IN AN MCDA CONTEXT: EXISTING METHODS - NEW RESULTS

Janssen MP[1], Koffijberg H[2]

[1]*University Medical Center Utrecht, Utrecht, The Netherlands,* [2]*University Medical Center, Utrecht, The Netherlands*

OBJECTIVES: Health technology assessment typically involves consideration of multiple conflicting criteria. Therefore, trade-offs are required between different objectives such as maximizing health, restricting budget impact, increasing health equity and maximizing safety. Methods such as multiple decision criteria analysis (MCDA) are therefore increasingly being used to reflect such trade-offs in a transparent and consistent manner. Although MCDA can be combined with cost-effectiveness analysis it may, however, invalidate results from Value of Information (VOI) analysis when it also includes other health-related or cost-related objectives. **METHODS:** In two case studies we first applied VOI methods directly and only to cost-effectiveness estimates, and then also applied these methods separately to all relevant decision criteria. In a simulation study on two drugs we calculated the expected value of perfect information (EVPI) with drug selection concerning a trade-off between cost-effectiveness and drug safety. In a clinical study on the primary prevention of cardiovascular disease using improved versus standard risk prediction we calculated the EVPI with selection of the best risk prediction strategy concerning a trade-off between cost-effectiveness and budget impact. **RESULTS:** In our simulation study we found EVPI estimates per patient based only on cost-effectiveness were up to € -586 lower and € +459 higher compared to EVPI estimates also acknowledging the safety criterion, depending on its weight. In our clinical study, the EVPI estimates based only on cost-effectiveness were consistently lower, up to € -540 per patient, compared to EVPI estimates also acknowledging the budget impact criterion. **CONCLUSIONS:** When decisions are based not only on cost-effectiveness but on other criteria as well, some of which also relate to costs or health effects, standard VOI estimates are no longer valid. However, separate application of VOI methods to each of the relevant decision criteria is straightforward and can facilitate transparent research prioritization in a complex MCDA context.

PRM230

A STATISTICAL MODELING FRAMEWORK TO CHARACTERIZE THE IMPACT OF PROGRESSION ON SURVIVAL IN ONCOLOGY

Ishak KJ

Evidera, St-Laurent, QC, Canada

The benefits and value of new cancer treatments often focus on the overall survival (OS) gains that patients may derive. Trials are typically not long enough to allow detailed understanding of OS, and potential benefits must be inferred from benefits on progression-free-survival (PFS). This raises questions such as whether early or later progression impacts survival, whether the increase in mortality following progression is sustained or gradually diffused, and whether a benefit observed on PFS implies a benefit in OS. Answering these questions requires an analytical framework in which progression and survival can be analyzed together and parameterized to address key questions. We propose a statistical modeling framework based on Cox regression and time-dependent predictors and effects. A simple formulation of this model would include a time-dependent indicator for progression, whose coefficient would measure the increase in risk of death following the event. This is very limiting, however; it assumes that the timing of progression does not matter and that the increase in risk of death is sustained indefinitely. A more flexible formulation can be built using two descriptors of event: the timing of progression (TP) and time since progression (TSP). These can be continuous measures or categorized (e.g., early vs. late TP), as appropriate. The coefficient for TP reveals whether later progression is associated with higher/lower subsequent mortality, while the coefficient of TSP reflects whether and for how long the increase/decrease in mortality is sustained and whether it ever returns to the level of patients who had not progressed. The impact of treatment can be captured on each of these parameters separately. The proposed framework will be illustrated with an example, and extension of the approach to other applications (e.g., measuring the impact of a stroke on survival) will be discussed.

PRM231

TOWARDS INTEGRATION OF RESEARCH EVIDENCE ON PATIENT PREFERENCES IN COVERAGE DECISIONS AND CLINICAL PRACTICE GUIDELINES: A PROPOSAL FOR A TAXONOMY OF PREFERENCE-RELATED TERMS

Utens CM[1], Joore MA[1], van der Weijden T[2], Dirksen CD[2]

[1]*Department of Clinical Epidemiology and Medical Technology Assessment, Maastricht University Medical Centre, Maastricht, The Netherlands,* [2]*Department of Family Medicine, CAPHRI School for Public Health and Primary Care', Maastricht University, the Netherlands, Maastricht, The Netherlands*

Despite the availability of a large body of research evidence on patient preferences for health outcomes and/or health care services, its use in health care policy decisions is limited. This contrasts with the current increasing attention for patient-cen-

tred care and integration of the patient perspective in health care policy decisions. A major challenge for the integration of evidence on patient preference is that research on patient preferences is performed by various disciplines (e.g. psychology and economics) that do not share a common language. It has been recommended to perform conceptual and taxonomic work on the definition and conceptualisation of 'preference' and related terms. The aim of this study was to develop a taxonomy of preference-related terms. The taxonomy was developed in three steps: 1) the identification of preference-related terms; 2) providing all identified terms with a definition from the dictionary; and 3) the identification of dominant theories or models from (health) economics and psychology that deal with the reference-related terms. The proposed taxonomy consists of several building blocks that hold all identified preference-related terms and demonstrate the relation between terms. The building blocks are centred around a factual event. Ex ante to this factual event lies building block 1, "decision making" holding terms like "choice" and "decision". Ex post lie building block 2 "evaluation process" and building block 3 "outcome of evaluation process". Building block 3 holds terms like "utility", "quality of life" and "satisfaction". Building blocks 1-3 are influenced by building block 4 "the value system". This value system is divided in cognition, affect and conation and holds terms like "beliefs", "expectation", "attitudes", "desires" and "intention". In this taxonomy, preferences can be considered as a part of the value system. The proposed taxonomy is a first step towards conceptual clarity to facilitate the integration of research evidence in health care policy decisions.

PRM232

WHEN IT MAY NOT BE NECESSARY TO MODEL OVERALL SURVIVAL FOR ECONOMIC EVALUATIONS OF ANTI-CANCER DRUGS

Hoyle M[1], Hamilton W[1], Rudin C[2]
[1]*University of Exeter, Exeter, UK,* [2]*Royal Devon & Exeter Hospital, Exeter, UK*

Overall survival (OS) is traditionally modelled in economic evaluations of anti-cancer drugs. However, OS is commonly associated with problems such as immaturity of the data, or confounding due to treatment switching or use of inappropriate treatments after progression. Fortunately, analysis of historical trials reveals that there is good evidence across a range of cancers that the mean time in post-progression survival (PPS) is equal between treatment arms, i.e. ΔPPS = 0. Therefore, we recommend that the default position is to assume equal mean times post-progression. If there is no a priori biological reason to suppose that the PPS times are likely to differ between treatments (e.g. due to differences in cross-resistance or long term toxicities between treatments), our recommendation is that it should be assumed that the mean time in progressive disease is equal between treatment arms if any of the following apply: OS is very immature; treatments post-progression are substantially imbalanced between treatment arms; in particular, treatment switching has occurred at progression; treatments post-progression are different to those routinely given in clinical practice; only single arm trials are available. If none of the above apply, or if there are a priorireasons to suggest that ΔPPS differs from 0, then the recommendation is to model OS and PFS in the traditional way. For chronic cancers, it is recommended that analyses should either assume equal times post initial treatment or equal time post progression. The assumption that ΔPPS = 0 substantially simplifies the economic analysis because cost-effectiveness becomes insensitive to OS. The methodology has been endorsed twice by NICE appraisal committees in assessments of drugs for chronic myeloid leukaemia. The cost-effectiveness of several drugs recently assessed by NICE are re-calculated using the methods proposed. Next, we give simplified formulae for the maximum drug price acceptable for reimbursement under the methodology.

PRM234

FEASIBILITY OF CONDUCTING RETROSPECTIVE STUDIES USING HASHTAGS AND SOCIAL MEDIA DATA FROM FACEBOOK AND TWITTER

Volovyk A[1], Topachevskyi O[2]
[1]*Hashtago, Kiev, Ukraine,* [2]*Digital Health Outcomes, Brussels, Belgium*

Various online services such as Socialbakers, Keyhole, Gnip offer tools to analyze, fetch and collect data from social media. This data is often presented in a form of interactive web based dashboards, displaying various trends: number of posts, mentions, shares, likes over time. Facebook and Twitter have an API to access data on social media profiles of real people. Users profiles usually have data on age, sex, employment and relationships status, specific group membership, etc. We conducted a simple feasibility study using Facebook API in diabetes area using profiles of people posting hashtags as a primary source of data. We then expanded the sample by adding people who liked, shared and reposted messages containing diabetes relaed hashtags #Diabetes, #dedoc, #ourD. We applied exclusion criteria to derive a sample consisting of patients only, hence targeting specific group of people. Our assumption was that people who interact with posts containing specific hashtag have diabetes. We used descriptive statistics to characterize obtained sample (n=17296) by calculating mean age, age distribution histogram, proportion of males and females and other descriptive metrics. We also calculated conditional probabilities of being in multiple disease area Facebook groups such as obesity groups or groups of people with increased risk of cardiovascular disease. Future area of research will be concentrated on aspects of in-degree centrality in network of diabetic people, hypothesis testing between two different groups, analyses of changes in positive/negative posting trends following drug launch, locating agents and influencers in the network and conducting prospective studies in social media using hashtags. Social Media data can be a valuable addition to a real life post launch data. Evidence on changes in positive/negative postings can be used as an additional piece of information in Phase IV studies or risk-sharing agreements.

PRM235

A FRAMEWORK FOR THE ECONOMIC EVALUATION OF SEQUENTIAL THERAPIES FOR CHRONIC CONDITIONS

Tosh J, Stevenson M, Strong M, Akehurst R
University of Sheffield, Sheffield, UK

Cost-effectiveness models often require the consideration of a sequence of treatments. This enables the downstream implications of a treatment to be captured, and alternative sequences to be compared. However, when many treatments are available, the number of feasible sequences can be large. Also, if the objective is to maximise net benefit for a given ICER threshold, then a comparative analysis to identify the optimal sequence may not be possible. This is further compounded when using individual patient simulation (IPS), because of the increased computational burden compared with cohort approaches. The aim of this study was to undertake a systematic review of optimisation methods that are applicable to a treatment sequencing IPS model. 28 key papers were identified across a range of academic subjects. Metaheuristics including simulated annealing, tabu search and genetic algorithms have been applied to simulation-optimisation problems and a bespoke review framework was applied to determine their appropriateness. Based on the review, a framework for the economic evaluation of treatment sequences was developed. The framework considers the requirements of a cost-effectiveness model to efficiently evaluate sequences, the application of the reviewed metaheuristics to determine the optimal sequence, and the consideration of these results within a decision-making context. This will be applied to a case study in rheumatoid arthritis. Alternative metaheuristic algorithms will be applied in an attempt to estimate a (near) optimal treatment sequence. Preliminary results of these experiments will be available in time for the November 2014 ISPOR conference. If these methods prove successful and feasible, then the framework may have potential applicability to sequencing models in many diseases. Whether there is the capability for it to be applicable within the current process for decision-making organisations such as NICE remains an open question, however, identifying an optimal sequence in a decision problem is of interest to decision makers.

PRM236

NOVEL INDIRECT COMPARISON METHODOLOGY FOR ESTIMATING TIME-DEPENDENT RESPONSE TO ANTIMUSCARINICS FOR THE TREATMENT OF OAB

Snedecor SJ, Sudharshan L
Pharmerit International, Bethesda, MD, USA

BACKGROUND: Common indirect treatment comparison (ITC) methodology in overactive bladder involves combining absolute reduction in urge urinary incontinence (UUI) episodes at study endpoint (e.g., week 12) to estimate the overall treatment effect. Trials with differing endpoints must assume equivalence to be included in the network. Further, analyses of endpoint data are not sufficient to predict efficacy at intermediate time points (e.g. 4 or 6 weeks). We developed and tested an alternate methodology to utilize available intermediate time points into an ITC of published studies of fesoterodine and tolterodine. **METHODOLOGY:** Study-level mean UUI reduction over time can be represented as the percent reduction from baseline, which can be modeled as a monotonically-increasing function with a theoretical maximum of 100%. This function is expressed with two parameters: $\%red = b_i * time/(c_i + time)$, where b_i is the maximum possible reduction for treatment i, and c_i is the time required to reach half the maximum reduction. The inverse *%red* is a linear function of *1/time* that can be used within a Bayesian ITC framework to generate a placebo-adjusted indirect comparison of efficacy. **CONCLUSIONS:** The endpoint results obtained from the alternate methodology were comparable to those obtained from an endpoint ITC. This novel methodology has the additional advantage of utilizing all available time point data within a single analysis, which can then be used to generate efficacy estimates at intermediate time points, which may be utilized within economic models. Limitations include unavailability of uncertainty estimates of the *%red* variable and difficulty of estimating combinations of parameters within functional constraints. Finally, our alternate methodology may be used for any longitudinal data exhibiting a monotonic increase or decrease and may be expanded to include a network with multiple treatments.

PRM237

BAYESIAN MODELS FOR COST-EFFECTIVENESS ANALYSIS IN THE PRESENCE OF STRUCTURAL ZERO COSTS

Baio G
University College London, London, UK

Bayesian modelling for cost-effectiveness data has received much attention in both the health economics and the statistical literature, in recent years. Cost-effectiveness data are characterised by a relatively complex structure of relationships linking a suitable measure of clinical benefit (\eg QALYs) and the associated costs. Simplifying assumptions, such as (bivariate) normality of the underlying distributions are usually not granted, particularly for the cost variable, which is characterised by markedly skewed distributions. In addition, individual-level datasets are often characterised by the presence of structural zeros in the cost variable. Hurdle models can be used to account for the presence of excess zeros in a distribution and have been applied in the context of cost data. We extend their application to cost-effectiveness data, defining a full Bayesian specification which consists of a pattern model for the individual probability of null costs, a marginal model for the costs and a conditional model for the measure of effectiveness (given the observed costs). The model is presented using a working example to describe its main features. In addition, we present a R package (BCEs0) that directly implements this framework and can be used to run a full Bayesian cost-effectiveness analysis of individual data in the presence of structural zero costs for some subjects.

PRM238

EFFECTIVE PRIORITISATION OF NATIONAL HEALTH TECHNOLOGY ASSESSMENTS

Moran P, Harrington P, Ryan M
Health Information and Quality Authority, Dublin, Ireland

Prioritisation of assessment topics is an essential activity within HTA. Failure to successfully identify technologies that are likely to have the greatest impact on the health system carries an opportunity cost that is measured in poorer decision